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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/997,551

11/27/2001

Jian-Dong Li

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07/13/2004

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EXAMINER

ZARA, JANE J

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/997,551

Applicant(s)

LI ET AL.

Examiner

Jane Zara

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 5-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 21 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3-19-02</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office action is in response to the communications filed 5-10-04.

Claims 1-22 are pending in the instant application.

This application contains claims 5-20 drawn to an invention nonelected in the reply filed on 11-10-03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Response to Arguments and Amendments

The declaration under 37 CFR 1.132 filed 5-10-04 is insufficient to overcome the rejection of claims 1-4, 21 and 22 based upon 112, first paragraph as set forth in the last Office action for the reasons set forth below.

Claims 1-4, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro inhibition of p38 MAP kinase following administration of pyridinylimidazole compounds, whereby Nontypeable

Hemophilus influenzae (NTHi) cytoplasmic protein induction of mucin (MUC5AC) transcription is inhibited, and for the in vivo inhibition of MUC5AC overexpression in the lungs of mice comprising the intraperitoneal administration of SB203580 before inoculation of NTHi, does not reasonably provide enablement for the reduction of MUC5AC overexpression in any mammal comprising the administration of any inhibitor of p38 MAP kinase in vivo for the reasons of record set forth in the Office action mailed 2-6-04.

Applicant's arguments filed 5-10-04 have been fully considered but they are not persuasive. Applicants argue that the pharmacological effects of pyridinylimidazole inhibitors of p38 MAP kinase in vivo are well studied and described in the art and several clinical trials in humans are underway for various diseases. Contrary to Applicants' arguments, MUC5AC induction involves several different signaling cascades and it is unclear in the art whether inhibition of the MUC5AC induction using p38 MAP kinase inhibitors is predictable in vivo. Induction of MUC5AC expression is thought to occur via various mediators of chronic inflammation, including, but not limited to IL-5, IL-9, IL-13 and TNF-alpha. MUC5AC induction, which in turn leads to mucin overexpression, involves synergistically acting inflammatory mediators, including IL-4, IL-5 and IL-9. IL-9, for instance, involves JAK/STAT signaling pathways, as opposed to p38/RK signaling cascades. These inflammatory mediators act inter- and intracellularly, further complicating the situation in vivo. In addition, host inflammatory responses also involve induction of IL-8, which in turn activates several members of the MAPK family cascade, including the p38/RK and SAPK/JNK1 cascades. The involvement of the

various cytokines and various signaling cascades in MUC5AC induction render the ability to reduce induction of MUC5AC expression in vivo using the instantly claimed p38 kinase inhibitors unpredictable.

The declaration of Dr. Li filed 5-10-04 teaches the ability to inhibit p38 MAP kinase induction of MUC5AC expression in vivo upon intraperitoneal administration of SB203580 in a BALB/c mouse model of Nontypeable Hemophilus influenzae before inoculation of NTHi. It is unclear, however, how this administration of the inhibitor SB203580 (in vitro or) in vivo before the inoculation of NTHi in the BALB/c mouse model is representative of the ability to inhibit induction of MUC5AC (over)expression after onset of Nontypeable Hemophilus influenzae using this or any p38 MAP kinase inhibitor (e.g. is SB203580 representative of the ability to successfully deliver and inhibit this MAPK using any p38 MAP kinase inhibitor, and including after onset of MUC5AC overexpression by p38?). For these reasons, the scope of enablement rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

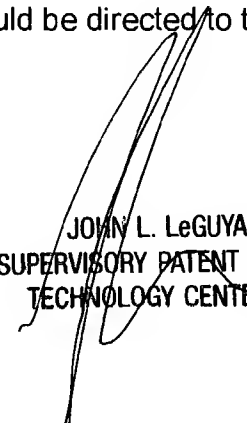
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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ
7-5-04


JOHN L. LeGUYADER
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